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THE EFFECTS OF STILBOESTROL ON THE SURFACE SEBUM AND UPON ACNE VULGARIS.

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DURING the past twenty years the relationship between acne vulgaris and the oestrogen content of the blood and urine has been investigated, and clinical trials of the therapeutic effects of oestrogens in this disease have been undertaken.

Wile, Barney and Bradbury (1939) estimated the urinary oestrogen output in twelve female acne patients and twenty controls. The average oestrogen output in the acne patients was 4.1 rat units per litre, compared with 7.7 in the controls.

Later, Wile, Snow and Bradbury (1939), using an improved method of estimation, found an increased androgen/oestrogen ratio in acne patients as compared with the controls.

Other workers have also investigated various aspects of the hormone content of blood and urine in this condition (Rosenthal and Kurzrock, 1933; Rosenthal and Neustaedter, 1935; Cornbleet and Barnes, 1939; Sorba, 1939; and Hamilton, 1941).

Therapeutic effects in acne patients treated with oestrogens have been reported by Van Studdiford (1935), Hollander and Schmitt (1939), Lawrence and Werthessen (1942), Simon (1945), Goeckerman (1950), Sulzberger and Witten (1951), Andrews *et al.* (1951), and Holbrook (1953).

Most writers have reported good results in both sexes. Some have used very small dosages, such as 0.5 mg. of stilboestrol a day for 10 days a month, and one would be surprised if this dosage had any influence on acne.

Whitelaw (1951) observed good results in male acne patients treated with local oestrogens over prolonged periods. The effect in females was not so marked.

The present author has given oestrogens in the form of stilboestrol 5 mg. a day for 21 days to a series of 23 male and 20 female acne patients. In the latter, the oestrogen was given without reference to the menstrual cycle; at the end of the hormone treatment patients were asked whether they had experienced any menstrual upset and only one patient complained of a disturbance of her cycle. In both sexes there was marked clinical improvement in 75% of cases. In no case were there any serious side-effects, and in none of the patients was it necessary to stop treatment before the end of the three-week period. Although the disorder tended to relapse after cessation of treatment, improvement could be maintained and eventual clearing achieved by following the hormone therapy with ultra-violet irradiation. It was noted both in the above series and in the present group of patients that response to ultra-violet light was much more dramatic in patients who had received oestrogens than in those who had not.

White and Lehmann (1952) found no improvement following oestrogen therapy; this is not surprising, since the dosage used was small—never more than 2 mg. daily. Moreover other methods of treatment such as antibiotics, diet, local applications and manipulative procedures were carried out on the oestrogen-treated series and on the controls and this would make the evaluation of the hormone treatment difficult. It is interesting that side-effects were common in this series with small doses over prolonged periods of up to 77 days; as mentioned above, larger doses of 3 or 5 mg. daily for periods of 21 days are relatively free from all side-effects, including menstrual upsets.

In the present series no difference was found in the 17-ketosteroid output in male or female acne patients from that of controls. This is in agreement with Becker (1953). White and Lehmann reported a depression of the 17-ketosteroid output as a result of oestrogen therapy, and their initial values were normal; but the statistical significance of their results is not above doubt.

EFFECTS OF OESTROGENS ON SERUM LIPIDS.

Another aspect of the action of stilboestrol was reported by Eilert (1953). She noted effects on the serum lipids in female patients treated with 0.5 or 1.0 mg. of stilboestrol daily, or with ethinyloestradiol in doses of 0.05 mg. daily. She recorded a depression of the serum cholesterol and an elevation of the serum lipid-phosphorus, and thus a depression of the cholesterol/lipid-phosphorus ratio. Although the lipid-phosphorus elevation was not significant statistically, nevertheless the cholesterol depression was quite definite. Her work is of interest in that it demonstrates an alteration of the fat metabolism by oestrogens, and further investigation of this problem may shed some light on the mode of action of these hormones in acne. On the other hand, Glass *et al.* (1953), using small doses of oestrogens, were unable to detect any change in the blood lipids.

EFFECTS OF OESTROGENS ON THE SEBACEOUS GLANDS.

Hooker and Pfeiffer (1943) were the first to report a reduction in the size and number of the sebaceous glands of rats following the injection of oestradiol monobenzoate.

Ebling (1948) investigated the effects of oestradiol, testosterone propionate, and progesterone on the sebaceous glands of female rats. He found that 100 μ g. per day of oestradiol for 36 days caused atrophy of the sebaceous glands; 1 μ g. per day had a definite but less marked effect. Testosterone, 1 mg. a day, increased the activity but not the number of sebaceous glands. There was no evidence that progesterone had any effect on them. Further work (Ebling, 1951) with oestrogens confirmed these findings. Prolonged oestrogen administration in the form of implants caused a decrease in sebaceous cell counts, and in the mean alveolar counts. However, in this series he recorded the interesting observation that there was an increase in the sebaceous cell counts during the first two days, followed by a progressive decrease on the third, fifth, and ninth days to a level on the twentieth day much below normal. Four cases in the present series were examined on the second day of treatment and in only one case (case 6) was there any evidence of this stimulating effect of oestrogens (Fig. 6).

Ebling's observations on the stimulating activity of these hormones is of interest in view of Bullough's (1946) findings that oestrogenic substances cause increased mitotic activity. Ebling (1954), when studying changes in the sebaceous glands during the oestrous cycle in rats, suggested that oestrogenic stimulation initially increased both the incidence of mitoses and gland size, but that subsequently the rate of cell-loss was so accelerated that even if mitotic activity remained high there was nevertheless a decrease of the sebaceous tissue. He discusses the possible modes of action of oestrogens and points out that they may act either through the pituitary or through the suprarenal glands. Speert (1940) showed that the local application of oestrogens to the mammary glands of monkeys caused proliferation of the treated gland only, and concluded this was evidence against any central action. In another paper Ebling (1953) points out that the decrease of sebaceous tissue due to oestradiol monobenzoate seems to be independent of the pituitary, since it can be produced in hypophysectomized rats.

Recently Haskin *et al.* (1953), using white rats, confirmed Ebling's findings with testosterone. They found an increase of 400% in the size of the sebaceous glands after 1 mg. of testosterone daily. In the case of progesterone, in contrast to Ebling's results, they reported a significant increase (360%) in the size of the sebaceous glands after giving 10 mg. daily for 15 days. An increase of 80% was also noted after giving ACTH, 0.5 mg. daily. They suggested that progesterone may be related to the pathogenesis of acne vulgaris in the female.

The methods employed by these workers, however, are not suitable for investigating the effects of hormones on the human sebaceous glands. A less direct method has to be employed and it was thought that an estimation of the surface sebum would be an index of the activity of the sebaceous glands.

METHODS OF SURFACE SEBUM ESTIMATION.

Various methods of estimating surface sebum have been employed; many of these have been either inaccurate or very time consuming.

Emanuel (1936, 1938) described his chamber method of collecting surface sebum. He used gravimetric estimation, and reported that in a given area the surface fat might vary up to 30%, but constantly found much more fat on the forehead than on the back, and a faster rate of "regeneration" of surface fat in the high-fat areas than in the low-fat areas.

Butcher and Parnell (1947) studied the sebaceous secretion on the human head. The fat was estimated by Bloor's nephelometric method.

Kvorning (1949) described his method of estimating fat by the manometric determination of the liberated carbon dioxide after wet combustion of a sample of lipids.

MacKenna *et al.* (1950) estimated the surface fat from the arm. Quantitatively they employed the gravimetric method. Further qualitative and quantitative studies of surface fats were carried out by Hodgson-Jones and Wheatley (1952). Hodgson-Jones *et al.* (1952) reviewed methods of fat collection and estimation, and reported quantitative details of the amount of fat in different areas.

Prose *et al.* (1952) found a higher surface fat in acne patients compared with controls, and a decrease following x-ray therapy.

Jones (1950) described a new method of determining minute amounts of fat based on the spreading effect of fatty acids on a monomolecular oil film. The area of the sebum-spread is directly proportional to the amount of sebum placed on the oil layer. Later Jones *et al.* (1951) used this method for the study of the rate of secretion of sebum. Various methods for collection of sebum samples were compared. They concluded that the direct application of solvent to the test area was the most efficient method, especially if combined with gentle rubbing. They also gave absolute values for the sebum-spread on a monomolecular oil layer. Each molecule of a saturated fatty acid occupied 21 square Ångstrom units with an oil-film pressure of 20 dynes per centimetre. The cholesterol molecule occupied 40 Å². Skin fat is a mixture of lipids and it was calculated that 0.19 µg. of fat gave a spread of 1 cm². Thus the sebum-spread can be readily translated into absolute figures.

Lorenz *et al.* (1952) used a modification of this procedure. They collected the surface fat by means of a glass rod which was applied to the skin at a

standard pressure measured with a von Frey algometer. The rod was then dipped into the oil film and the sebum-spread measured. They found an increase in the surface fat when the patient was in a warm environment and a decrease in cool surroundings. Marked fluctuations were also recorded in day-to-day observations. They also give an account of the apparatus used by Jones.

This sensitive method of Jones has been employed with slight modifications in the present investigation. It is a relatively simple procedure and estimations can be performed quite rapidly.

INVESTIGATION.

This investigation was undertaken to ascertain whether any change could be detected in the surface sebum following the oral administration of stilboestrol. The dose given was 3 mg. a day and from previous experience this was known to improve acne vulgaris. Four male and two female acne patients were used in this series. Four patients were admitted to the dermatological wards; two were out-patients, both intelligent undergraduates of University College, London, who were willing to co-operate in the exact timing of cleansing their skins and presenting themselves for the collection of samples. As both the latter were working close at hand their skins were not exposed to the weather during the test periods.

In three cases stilboestrol was given in doses of 1 mg. thrice daily for 21 days. In one patient (Case 3) treatment was stopped after 11 days because of nausea and headaches. After two days, treatment was resumed with 1 mg. daily and continued for a further 18 days without any side-effects. In Case 2, 3 mg. of stilboestrol was given daily for 11 days and treatment was stopped because the patient wished to return home for domestic reasons. Case 6 was treated with 3 mg. a day for 26 days, but because the clinical response was slow the dose was increased to 5 mg. for a further 7 days.

In all patients the acne improved; Case 4 showed the most marked improvement and almost completely cleared during the exhibition of stilboestrol. In all cases, the acne finally became inactive after the oestrogen therapy had been followed up with ultra-violet irradiation.

Method of Surface Sebum Estimations

Bottles of 20 ml. capacity with a narrow neck, diameter 1.4 cm., were used for the collection of sebum samples. The area of their apertures was standardized by measuring their imprint on graph paper. The bottles were then labelled so that the same bottle was used for sampling any given area. Thus all samples from a given site in any one patient were constant in respect of the area of skin exposed to the solvent.

The sebum solvent used was petroleum ether (Analar, boiling range $40^{\circ}\text{C}.$ – $60^{\circ}\text{C}.$). The amount of solvent measured into the bottles was in proportion to the sebum density of the sampled region. Thus 1 ml. was used for the back and 2 ml. for the forehead and nasolabial region; since the back has approximately half as much surface sebum as the face, this gave a solution of fats from these areas of about the same concentration. The petroleum ether was carefully measured by means of a pipette which had been washed several times with the solvent. The bottles had previously been thoroughly cleansed with ether followed by petroleum ether. They were corked immediately after receiving the measured quantity of solvent.

The patients' skin was prepared 5 hours before sampling, by swabbing the area four or five times with ether. The selected area on the back was covered with a metal cap about 4 cm. in diameter held in position with adhesive plaster so as to prevent the test area from being rubbed by garments or bed clothes. No protection was applied to the forehead or nasolabial sites, but a large area of skin was cleansed so that there was no danger of sebum flow from the un-cleansed parts into the sampling site. The patients were warned not to touch the cleansed areas during the subsequent 5 hours. At the end of this time the selected sites were sampled. The appropriate bottle containing the solvent was inverted on the test area, and with practice and co-operation of the patient this could be accomplished without spilling any of the petroleum ether. The solvent was left in contact with the skin for 30 seconds; gentle agitation while the neck of the bottle was kept firmly applied to the skin ensured a reasonably thorough removal of the sebum. The bottles were then rapidly recorked to prevent any loss of solvent by evaporation.

In most patients three or four regions were sampled at the same time. Samplings were repeated at about 3-day intervals before and during the period of oestrogen therapy. In two cases sampling was continued after stilboestrol therapy ceased.

It was found that with the quantity of solvent used (1 ml. for the back, 2 ml. for the face areas) 0.05 ml. of this sebum solution has a satisfactory spread when placed on the oil film. This quantity was measured with a tuberculin syringe, the same part of the barrel being used for all estimations. The sebum solution was drawn up to the first 0.05 ml. mark and was then allowed to fall drop by drop on to the oil film. This method ensured that the amount of sebum solution was accurate and constant (but perhaps not exactly 0.05 ml., which is immaterial). A tuberculin syringe was used because of the speed with which it could be manipulated; thus loss of solvent by evaporation was minimized during the removal of the sebum solution from the bottle.

The oil film was made by allowing a drop of oil to fall on to 0.3% sulphuric acid contained in a petri dish of 14 cm. diameter. The petri dish was coated with hard paraffin to a thickness of about 1 mm. The 0.3% sulphuric acid

was made up in distilled water and used at room temperature. The acid was poured into the petri dish which was placed on a tray on a levelling table. The petri dish was filled to above the level of its sides; this can be accomplished because of surface tension effects between the dilute sulphuric acid and the paraffin wax.

The oil used was "Edwards 8a high vacuum oil," heated to 300° C. for 8 hours before use. One drop of oil delivered by an intracutaneous needle was sufficient to cover the whole surface of the dilute sulphuric acid.

When the 0.05 ml. of sebum solution was dropped on to the oil film, a spreading effect developed as the petroleum ether evaporated. When the spread had become stabilized the area was outlined on a glass plate placed above the oil film. This tracing was transferred to a sheet of paper and its area measured with a planimeter. Two planimeter readings for each area were taken and the average recorded.

Each sample was estimated three times and the average calculated. This result was taken as the final reading and expressed as sebum-spread in square centimetres.

All readings were related to 1 ml. of solvent. Thus if 2 ml. of solvent had been used the resulting sebum-spread was multiplied by 2. All readings therefore are comparable, no matter what original dilution was employed.

RESULTS.

A brief outline of the progress of each of the patients undergoing hormone therapy is given. The changes in surface sebum are shown graphically in Figs. 1-6.

The results are expressed in the observed sebum spread and are not shown as absolute figures, since the apparatus was not calibrated for absolute readings. The readings are however strictly comparable.

In most cases three pre-treatment estimations were made; from these was calculated an average and the degree of variability dependent upon experimental error and natural variation. With these factors the post-treatment levels were compared.

The results were examined statistically and conclusions drawn from these observations.

Case 1.—A man aged 18.

Severe pustular acne of the face and back.

Sebum estimations were carried out before, during, and after stilboestrol treatment. The results are shown graphically in Fig. 1. It will be seen that both the forehead and back readings decreased during treatment.

After treatment ceased there was a tendency for the sebum of the forehead to return to pre-treatment levels. The surface sebum of the back, however, showed a much less marked upward trend.

The acne was clinically improved after about 2 weeks of treatment. After the cessation of hormone therapy ultra-violet light was given and led to further improvement.

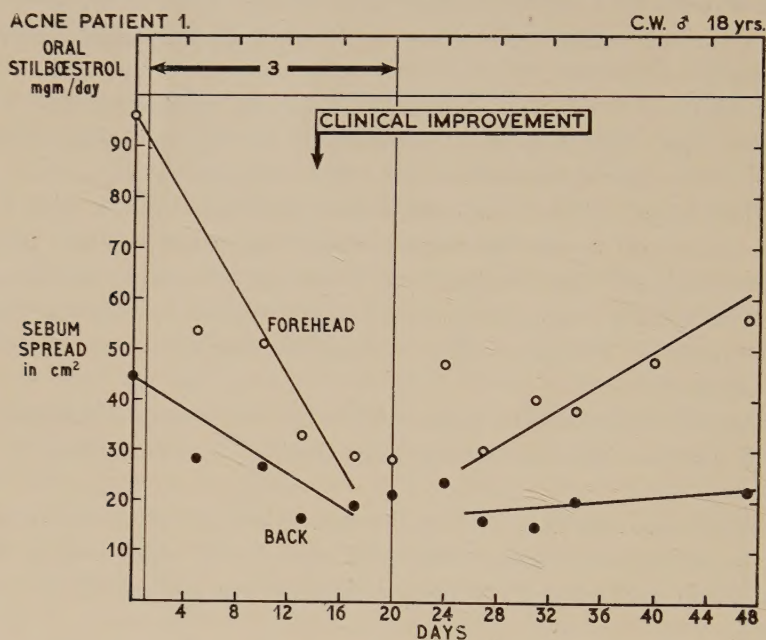


FIG. 1.

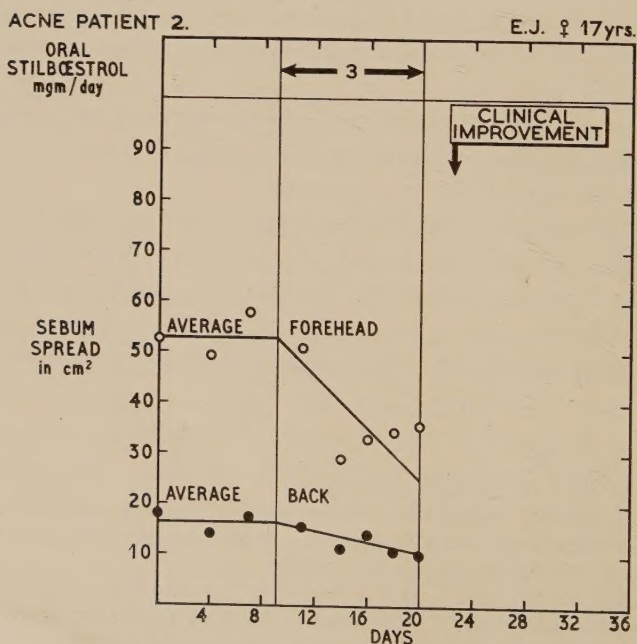


FIG. 2.

Case 2.—A girl aged 17.

Mild acne vulgaris of the face, with pustular lesions on the chin. She was admitted to the ward during the period of surface sebum estimations.

Stilboestrol, 3 mg. daily, was given for 11 days.

The treatment period was short because she wished to return home. At about the end of it, her face was very much better, and was completely cleared after eight exposures to ultra-violet light.

The surface sebum both of forehead and back was reduced as the result of treatment (Fig. 2).

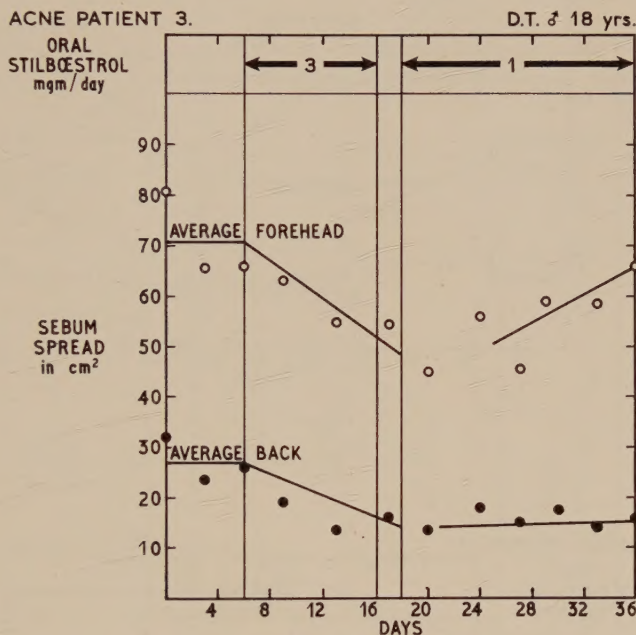


FIG. 3.

Case 3.—A man aged 18.

Mild acne of the face. The estimations were made as an out-patient before and during treatment. After 11 days' administration of 3 mg. stilboestrol daily, he developed nausea and headaches. The hormone was therefore stopped for 2 days.

It was then recommenced at 1 mg. daily. With this dosage there were no side effects, and no evidence of depression of the surface fat; in fact the surface sebum of the face began to increase (Fig. 3).

Nevertheless his acne did not deteriorate during the period of lower dosage, although improvement was not marked as in the two previous cases. He was given ultra-violet light at the termination of his treatment with good effect.

Case 4.—A man aged 18.

Severe acne of the face and back. After 21 days' treatment with stilboestrol, 3 mg. daily, all three sampled areas showed a decrease in their surface sebum (Fig. 4).

Marked clinical improvement occurred after the first week. After treatment ceased there was an upward trend towards pre-treatment levels (Fig. 4), most marked in the areas of highest sebum density. After 16 days these readings were stopped and the patient was given ultra-violet light. After six weeks of this treatment all activity of his acne had ceased.

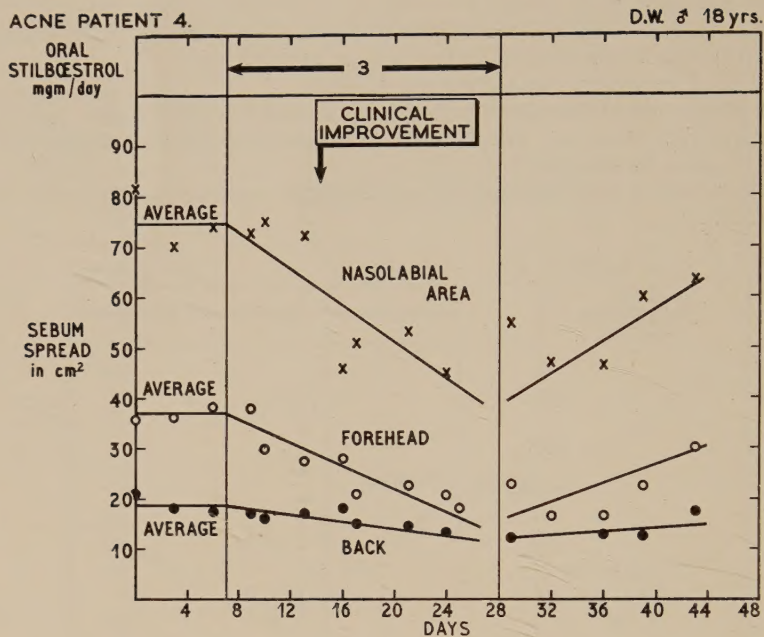


FIG. 4.

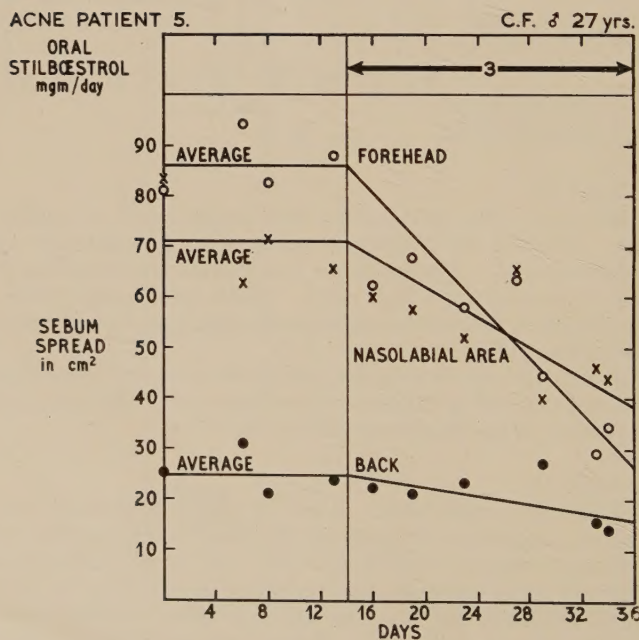


FIG. 5.

Case 5.—A man aged 27.

Long-standing acne of the face and back.

Readings were taken from the forehead, nasolabial area, and back before and during oestrogen therapy. Stilboestrol, 3 mg. daily, was given for 21 days. The surface sebum was depressed in all areas tested, most markedly in those of highest surface sebum density (Fig. 5).

There was some degree of improvement during treatment, and this was maintained, after stopping hormone therapy, by ultra-violet irradiation. After two months of this his acne finally cleared.

Case 6.—A girl aged 18.

Severe pustular acne of the face and back. Samples were taken from the forehead, nasolabial area and back, before and during stilboestrol therapy. Stilboestrol 3 mg.

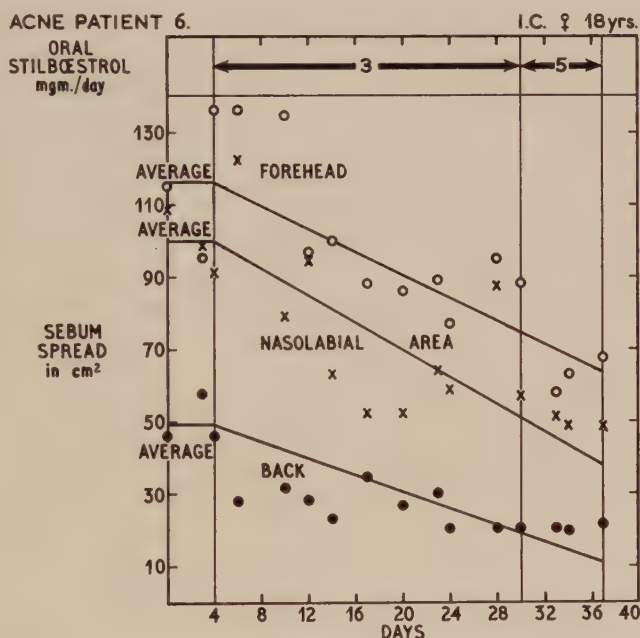


FIG. 6.

daily, was given for 26 days. During this time the face improved; but there was little clinical improvement in the condition of her back, in spite of a decrease of the surface sebum there (Fig. 6).

Because of the lack of improvement the dose was increased to 5 mg. daily for a further 7 days. This caused the surface sebum of the forehead to fall markedly; there was no further reduction in the sebum of the back, which nevertheless showed considerable clinical improvement.

After cessation of hormone treatment, ultra-violet light was given twice weekly to the affected areas. All activity of the acne ceased after two months' treatment.

Statistical Examination.

The results were examined by the Statistical Department of University College, London.

All regions examined in all patients showed a significant decrease in the surface sebum with the exceptions of the back in Case 5 and the forehead in Case 3 (the latter patient was treated for a short period of only 11 days with 3 mg. a day).

Below is given the average initial sebum readings, the regression coefficients, and level of significance for each region sampled in all six patients.

<i>Case 1.</i>				Back.	Forehead.	
Average reading before treatment	.	.	.	44.5 cm. ²	96.1 cm. ²	
Regression coefficient	.	.	.	-1.216	-3.278	
Level of significance	.	.	.	Significant 5% level	Significant 5% level	
<i>Case 2.</i>				Back.	Forehead.	
Average reading before treatment	.	.	.	16.6 cm. ²	53.1 cm. ²	
Regression coefficient	.	.	.	-0.594	-2.019	
Level of significance	.	.	.	Highly Significant 1% level.	Significant 5% level	
<i>Case 3 (when given 3 mg. a day).</i>				Back.	Forehead.	
Average reading before treatment	.	.	.	27.0 cm. ²	70.7 cm. ²	
Regression coefficient	.	.	.	-0.940	-1.232	
Level of significance	.	.	.	Significant 5% level	Not significant	
<i>Case 4.</i>				Back.	Forehead.	Nasolabial area.
Average reading before treatment	.	.	.	18.6 cm. ²	36.5 cm. ²	74.9 cm. ²
Regression coefficient	.	.	.	-0.229	-0.986	-1.465
Level of significance	.	.	.	Significant 5% level	Highly significant 1% level	Highly significant 1% level
<i>Case 5.</i>				Back.	Forehead.	Nasolabial area.
Average reading before treatment	.	.	.	25.5 cm. ²	86.1 cm. ²	70.7 cm. ²
Regression coefficient	.	.	.	-0.387	-2.474	-1.136
Level of significance	.	.	.	Not significant	Highly significant 1% level	Significant 5% level
<i>Case 6.</i>				Back.	Forehead.	Nasolabial area.
Average reading before treatment	.	.	.	49.6 cm. ²	116 cm. ²	98.8 cm. ²
Regression coefficient	.	.	.	-0.742	-1.793	-1.601
Level of significance	.	.	.	Highly significant 1% level	Highly significant 1% level	Highly significant 1% level

The increase in sebum-spread after cessation of stilboestrol treatment in Cases 1 and 4 was examined statistically. In neither case was the increase significant; nevertheless the values are suggestive of a rise to pre-treatment levels.

In Case 3, after reduction of the dosage to 1 mg. daily, a significant rise to pre-treatment levels was observed (coefficient of increase + 1.191).

Relation between Pre-treatment Levels and the Rate of Decrease per day (Regression Coefficient).

The regression coefficient represents the rate of daily decrease of surface sebum. When the coefficients of regression for all regions tested in all patients are plotted against their corresponding pre-treatment levels a clear relationship is seen between them (Fig. 7). The graph indicates that the higher the pre-treatment level of sebum, the greater is the response to stilboestrol. Thus

generally the decrease in surface sebum is greatest on the forehead and nasolabial regions and least on the back.

With aid of this graph, the degree of fall for a given initial sebum density can be predicted when a patient is treated with 3 mg. of stilboestrol daily. For example, if the average pre-treatment sebum level is 70 cm² spread, then, from the graph, the daily expected fall is 1.6 cm²; after 10 days the reading should be $70 - (1.6 \times 10) = 54$ cm².

EFFECT OF ORAL STILBOESTROL ON THE SURFACE SEBUM

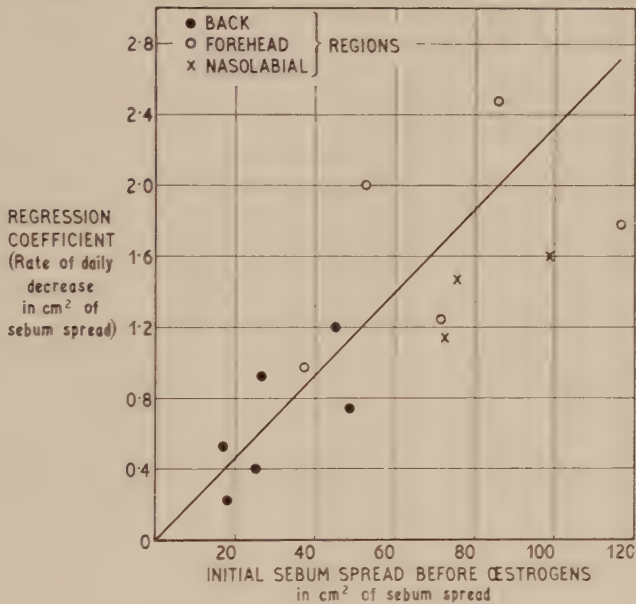


FIG. 7.

DISCUSSION OF RESULTS AND CONCLUSIONS.

It has been shown that stilboestrol in a dosage of 3 mg. a day causes a significant decrease of the surface sebum of the back, forehead and nasolabial areas.

The higher the initial sebum reading, the greater is the daily decrease, and the quicker the recovery rate when treatment is stopped.

Stilboestrol in adequate dosage has a beneficial but temporary effect on acne vulgaris, which tends to relapse subsequently unless other forms of therapy are instituted. After stopping oestrogen treatment ultra-violet light was used as a routine and cleared up the active lesions in all cases. The improvement was more rapid in patients who had been given stilboestrol than in those treated with ultra-violet light alone.

Although it appears that decreasing sebaceous secretion aids in the improvement of acne lesions, this may not be the direct operating factor. For it was

observed that when there was any degree of inflammation its retrogression sometimes lagged behind the sebum depression. Also, as the sebum level rose after stopping treatment it might be some time before the inflammatory phase again became established.

It is possible that oestrogens induce some *qualitative* changes in the sebum. In twelve cases, biopsies were made before and after oestrogen therapy, and sections stained for neutral fats, phospholipids, cholesterol and glycogen. They did not show any significant change, but these histo-chemical methods are crude and small changes would not be evident. Perhaps chromatography of the fatty acids of sebum would be of help in solving this problem.

Again, some alteration of the *physical* properties of sebum may be induced by oestrogens. If blocking of the follicle by a blackhead is an important mechanism in the production of acne lesions, then a decrease in the viscosity of the sebum would allow it to escape through channels that were previously impassable.

SUMMARY.

Oral stilboestrol improves cases of acne. A series of 23 males and 20 female patients is reported. Improvement occurred in 75% of both sexes; the mechanism of this is discussed. There is a tendency for the acne to relapse when treatment is stopped.

In six cases of acne vulgaris of varying severity, a significant reduction of the surface sebum has been demonstrated following the oral administration of stilboestrol. The rate of response depends upon the initial sebum level. The higher the initial level the greater is the daily decrease.

The amount of sebum tends to return to pre-treatment levels when hormone therapy is stopped, although in two cases tested these increases were not statistically significant.

Histochemical methods applied to biopsies taken before and after stilboestrol treatment failed to show any alteration in the nature of the fat in the sebaceous glands, or any significant change in their glycogen content.

I am greatly indebted to Dr. W. N. Goldsmith for his invaluable help, encouragement and advice with this investigation. I also thank Dr. A. Bigham in whose department at Bradford Royal Infirmary the early clinical trials were undertaken.

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OBSERVATIONS ON THE USE OF HYDROCORTISONE OINTMENT.

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IN clinical trials undertaken with a growing series of cases by Sulzberger and Witten (1952), Sulzberger, Witten and Smith (1953), and Sulzberger and Witten (1954), hydrocortisone ointment has been reported to be of value in a variety of skin disorders, particularly in atopic dermatitis (flexural prurigo), in conditions involving the eyelids, perianal and perivulval skin, scrotum, nipples and ears, and in contact dermatitis. (In a total of 252 cases they reported considerable improvement in 88 and moderate improvement in 73). Sulzberger and Witten state (1954) that in their considered opinion hydrocortisone ointment, properly and adequately applied, has proved to be the most effective topical medication they have ever used in the treatment of atopic dermatitis. Sulzberger (1954) summarizes their findings by saying that in many, but not all, dermatoses responding well to systemic cortisone, local hydrocortisone will bring about substantial morbidistatic effects, and that topical hydrocortisone shows promise of becoming one of the most useful external agents ever developed. No case in their series showed epidermal sensitization to hydrocortisone, nor systemic effects.

These investigators used ointments containing 1% and 2.5% hydrocortisone. Although four different ointment bases were employed, none was found superior in general to the others. Strengths of ointment greater than 2.5% did not produce much added improvement, but in some cases the 2.5% strength was more effective than 1%. Comparison between ointments containing hydrocortisone acetate and the free alcohol gave "little reason for preferring one to the other in the general run of cases" (Sulzberger and Witten, 1954). The ointments were applied two or three times daily, and the method of symmetrical paired comparison, using ointment base alone as a control, was adopted in most cases. Patients were seen at weekly intervals, but it was noted that in many improvement started within 48 hours of the start of treatment. It is stated that "only rarely did a favourable response follow an initial lag period of a few days to two weeks during which time the hydrocortisone was essentially ineffective. In such instances it was difficult to be certain that the delayed improvement was in fact due to the hydrocortisone."

A further series of 30 children suffering from infantile eczema treated with hydrocortisone is that of Witten *et al.* (1954) who recorded favourable responses

in 18 cases. Alexander and Mannheim (1953) reported favourably on the use of 2.5% hydrocortisone ointment in the treatment of 29 cases of pruritus ani, and concluded that it was a valuable aid in the treatment of this condition. Kanee (1954) reports that in contact dermatitis hydrocortisone offers great and immediate relief, and shortens the duration of the disease, while it is a promising though not a curative aid in atopic dermatitis. Robinson and Robinson (1954) have also reported favourably on the use of hydrocortisone in a large number of patients with various skin disorders.

By contrast Goldman and Preston (1953), who investigated the effects of different means of applying hydrocortisone locally to the skin, recorded disappointing results in 135 patients with a variety of skin disorders treated by applications of hydrocortisone ointments (in strengths from 0.1% to 5.0%) and concluded that on the whole the present type of ointment containing Compound F was ineffective. No details of the technique employed in application, or of the strengths of ointment used in individual cases were given, and there was no mention of a control series. (Sulzberger and Baer have subsequently noted, in a footnote in the *Yearbook of Dermatology* (1953/4) that Goldman has personally communicated that he had better results later).

In a well controlled series of 79 patients with rhus dermatitis, Eskind *et al.* (1954) found that in patients with the usual vesicular type of eruption there was no greater effect with hydrocortisone, used in various strengths, than with a control placebo, and remarked that for such cases it was valueless. There was, however, an excellent response in four patients with an angio-neurotic oedema pattern of reaction to poison-ivy.

Malkinson and Wells (1954), reporting a series of 71 skin cases treated with 2.5% hydrocortisone ointment, found that in nearly two-thirds the hydrocortisone had a positive effect compared with the control base, and of these one-quarter responded better to hydrocortisone than to any other application. They noted particularly good results in chronic otitis externa, eczema of the eyelids, and in some cases of pruritus ani. However, they remarked on the individual variation in response: some patients obtained a rapid and striking relief, but others with similar lesions responded not at all.

In view of the somewhat conflicting reports it was decided to attempt to assess the efficacy of hydrocortisone ointment with care in the series reported here, particularly as no accounts originating from this country were available. Its use has been confined in this investigation to (i) patients suffering from prurigo (atopic dermatitis) and infantile eczema; (ii) patients with affections involving muco-cutaneous junctions (pruritus ani, and eruptions around the lips—angular stomatitis and cheilitis exfoliativa); and (iii) patients with exogenous eczema due to epidermal sensitization (contact dermatitis).

In the patients with flexural prurigo and exogenous eczema, the symmetrically

paired comparison method of control was employed, the hydrocortisone being applied to one site, and a control ointment consisting only of the base being used on a contralateral or similarly affected site.

In many cases there were other affected parts which for further comparison were either left untreated, or treated with more orthodox measures.

In an attempt to eliminate personal factors in the assessment of results it was arranged that only the dispenser should know which areas were receiving the hydrocortisone and which the dummy base, and he dispensed these for right or left sides in a random sequence. The person assessing the effect on the case did not know which side had received the active ointment until the treatment was stopped, or in some cases where an obvious difference occurred, until at least a week after the start of treatment. For the same reason, the tubes used to contain the ointments were the same for both active ointment and control base, with plain labels marked simply, "for use on RIGHT arm," "for use on LEFT arm," etc.

The patients with pruritus ani, or affections of the lips, did not lend themselves to this method of paired comparison, and resort was made to supplying them with either the hydrocortisone ointment or the control ointment, and alternating the substance dispensed after an interval. Again, only the dispenser knew which ointment had been supplied. Some of the patients with lesions on the lips used the ointments under test on only one-half of the lips, and left the other half untreated as a further control.

The active ointments used contained 2.5 mg. and 1.0 mg. hydrocortisone acetate in 100 mg. base. All patients, except some of those with affections of the lips, started with the 2.5% strength, but after 1-2 weeks this was often reduced to 1%. In all cases applications were made twice daily and the ointment well rubbed in.

Although at the beginning the trial was confined to patients admitted to the ward for treatment, it was later realized that the mere fact of being at rest in hospital and being free from the responsibility of treating themselves resulted in much improvement in many patients without any specific treatment being given, and this introduced an imponderable factor into the assessment. Later many were treated as out-patients, to overcome this difficulty. Where control and active ointments were used simultaneously on two different areas by out-patients, careful instructions were given to confine the use of the ointments to the designated areas. This method is less reliable than having the patients in the ward, and because of this the results appertaining to in-patients and out-patients are tabulated separately. In-patients were seen daily, and out-patients once a week. Assessments were agreed upon between the writer and at least one other observer, both of whom were unaware which ointment was being applied.

The duration of treatment varied. At first, because of the reports of improve-

ment within 48 hours there was a tendency with in-patients to make a final assessment, and sometimes to change the treatment, after a relatively short period (especially in patients receiving a routine measure on a third area which was improving more than the test sites). Later, the treatment was continued for at least 10 days, and in many cases for many weeks. Photographs were taken to provide objective evidence of the condition at the start, and where apparent improvement occurred, during the course of treatment.

MATERIAL.

A total of 53 patients, with the following diseases, are reported here :

		In-patients.	Out-patients.	Total.
Group I	{ Flexural prurigo .	7	12	19
	{ Infantile eczema .	4	3	7
	{ Exogenic eczema .	6	4	10
Group II	{ Pruritus ani .	3	6	9
	{ Cheilitis exfoliativa .	—	5	5
	{ Angular stomatitis .	—	3	3

The patients with flexural prurigo were young adults with a history of the condition since childhood. The degree of severity varied in individuals, but there was a tendency to select for treatment those patients whose eruptions were fairly symmetrical, in whom the two sides could be easily compared. The duration of treatment of out-patients ranged from 2 to 14 weeks (average $4\frac{1}{2}$ weeks), and of in-patients from 10 days to 5 weeks (average $2\frac{1}{2}$ weeks).

The children with infantile eczema were treated as in-patients for 1 to 2 weeks, and as out-patients for 2 to 12 weeks (average 5 weeks).

The patients with exogenic eczema were treated with hydrocortisone for only limited periods up to 2 weeks. All were subjects whose eruptions and histories supported the diagnosis, and all cleared up in any case relatively quickly under general measures and removal from the cause. Positive patch tests were obtained in 8 patients as follows : Nickel (1), mercury (1), proprietary cosmetic (1), antihistaminic creams (2), procaine (1), penicillin (1) and proprietary fungicide (1). One other patient had an eruption clearly due to penicillin, but he was not tested because an intervening surgical condition necessitated his transfer. The remaining patient seemed obviously to be reacting to an agent encountered among testing materials in a dairy, but such patch-testing as was performed failed to bring it to light.

None of the patients with pruritus ani had any local or general abnormality apart from a mild intertrigo in some cases. As out-patients their treatment ranged from 3 to 8 weeks (average 5 weeks) and as in-patients (some of whom continued as out-patients) from 1 to 4 weeks (average 2 weeks).

No specific cause had been demonstrated in any of the sufferers from cheilitis. The duration of treatment ranged from 2 to 8 weeks (average 4 weeks).

Two of the patients with angular stomatitis had dentures which had allowed the corners of their mouths to droop. The third was sensitive to plastic dentures, but his condition had persisted even when these had been replaced by dentures made of material to which he was not sensitive. The duration of treatment ranged from 3 to 8 weeks (average 5 weeks).

It should be mentioned that many of these patients with flexural prurigo, pruritus ani and cheilitis had been treated in the past with other measures, but had derived no permanent benefit, or had recently relapsed.

RESULTS.

In assessing the results of local treatment there are many problems. Apart from the influence of rest in hospital, or of treatment with any new remedy, which factors are uncontrollable, there arises a difficulty in adequately classifying the degree of response. Although basically it is only required that the area treated should be compared with a control area, this alone provides nine alternative degrees of comparison, even where the simple designations—better, worse, or unchanged—are used. Although some of these alternatives are not important, both treatments may result in improvement, though one of less degree than the other, and this fact must be noted. Further, where it is possible to provide an added control by treating a third area with a different measure or by leaving it untreated (as was possible in many cases in this series) an additional, though useful, complication is introduced. Bearing these features in mind, it was decided, in those cases where a paired comparison method of control was possible, to use seven different classifications to tabulate the results in this series. Any scheme of tabulation is arbitrary, but it provides a simple method of collating and presenting the results. The classification adopted was :

- A. Improvement of hydrocortisone-treated area, without improvement of other areas.
- B. General improvement of all areas, but greater with hydrocortisone than with control or any third measure.
- C. General improvement of all areas, with no significant difference between hydrocortisone- and control-treated areas.
- D. No improvement with hydrocortisone but improvement on control area, or area treated with a third measure.
- E. No improvement of any area.
- F. Worse in all areas.
- G. Specifically worse in hydrocortisone-treated area.

This cumbersome classification seemed better than simpler forms because many patients showed general improvement, and often improvement in the control areas, while under treatment.

In those cases where alternation of control and treatment under test was

employed and paired comparison was not possible, the following classification has been used :

- A. Improvement when on hydrocortisone ; relapse or no improvement when on control.
- B. Improvement with both but of greater degree with hydrocortisone than with control.
- C. No improvement with either hydrocortisone or control.
- D. Worse when on hydrocortisone.

In both these classifications only those patients coming into Groups A and B can be interpreted as having shown significant improvement with hydrocortisone ointment, and only Group A improvement when other treatment had failed to have effect.

The results of treatment are summarized in Tables I and II.

TABLE I.—*Group I.*

Disease.	Number of patients.	Degree of response.						
		A.	B.	C.	D.	E.	F.	G.
Flexural prurigo (In-patients) .	7	. 0	1	3	1	2	0	0
(Out-patients) .	12	. 1	6	3	0	1	1	0
Infantile eczema (In-patients) .	4	. 0	0	1	0	3	0	0
(Out-patients) .	3	. 0	1	0	0	2	0	0
Exogenic eczema (In-patients) .	6	. 0	0	4	1	0	0	1
(Out-patients) .	4	. 0	2	2	0	0	0	0
Totals . . .	36	. 1	10	13	2	8	1	1

TABLE II.—*Group II.*

Disease.	Number of patients.	Degree of response.			
		A.	B.	C.	D.
Pruritus ani (In-patients) .	3	. 0	1	2	0
(Out-Patients) .	6	. 2	2	2	0
Cheilitis exfoliativa (Out-patients) .	5	. 3	0	2	0
Angular stomatitis (Out-patients) .	3	. 0	2	1	0
Totals . . .	17	. 5	5	7	0

DISCUSSION.

There is a suggestion from these figures that the results of treatment were better with out-patients than in-patients, but the total number of individuals involved does not seem sufficient to provide a basis for any useful statistical comparison. There were several patients in the total who failed to maintain an initial improvement fully, and who tended to relapse while under treatment. In collating the results they have nevertheless been placed in the highest category which they reached at any stage, and their *maximum* degree of improvement is therefore recorded despite the subsequent relapse.

Flexural Prurigo.

Out of 19 patients with flexural prurigo, there was significant improvement on those local skin areas treated with hydrocortisone in 8 instances. In many of the remainder there was general improvement in the condition, including the area treated with control base, but this could hardly be ascribed to the local action of the hydrocortisone on one limited skin area. There is not at present any evidence of systemic absorption of topically applied hydrocortisone (Smith, 1953). This illustrates one of the principal difficulties involved; some of these patients who improved generally were in a hospital ward, with its inevitable effect on their attitude and their disease, and the others could not fail to be aware that they were being treated with something which they had never had before. These two factors could not be avoided, but care was taken not to confuse the issue further with any treatment other than by local applications to the skin. Systemic cortisone and sedatives were not given, and at the stage when the investigation was in progress no great attention was paid to resolving any background factors of emotional or physiological stress, or to investigating any allergic aspects of the condition. In such a constitutional reaction as flexural prurigo it seems unreasonable to expect any dramatic improvement from a local ointment only. The fact that 8 patients with flexural prurigo did show some significant improvement with hydrocortisone when background factors were ignored suggests that in some cases it can be a useful adjunct to the therapy of the condition. The figures do not suggest however that used alone it is likely to be of great benefit. Only one of the patients with flexural prurigo showed a really impressive improvement, and none had complete resolution of their lesions. Three of the 8 who showed some degree of improvement relapsed several weeks later while still using hydrocortisone. One of these subsequently was rather better controlled with the 2.5% ointment than with the 1%.

Infantile Eczema.

In infantile eczema, to which the same considerations apply, there was significant improvement in 1 out of the 7 patients treated, and the same conclusions can be drawn as for the patients with flexural prurigo.

It is doubtless desirable to assess the effect of local hydrocortisone in conjunction with more general and analytical measures, but in the present investigation this would have introduced so many imponderable factors that the investigation would have been almost impossible to control.

Exogenic Eczema.

In the 10 patients with exogenic eczema only 2 showed significant improvement from the local use of hydrocortisone. The practical treatment of a specific contact reaction requires the removal of the offending external agent, and local

hydrocortisone would be of likely value only if it was effective with great rapidity, so as to tide the sufferer over an acute phase until the provoking agent had been eliminated. With exclusion of the responsible external agent, a contact reaction can be expected to be self-limiting within a short period in many cases. All 10 patients in this group had largely recovered within 2 or 3 weeks, and only 2 showed a slight hastening of resolution which could be ascribed to hydrocortisone. One patient became so much worse while using hydrocortisone that it was thought that she might have developed a sensitivity to it. Patch-testing with 2.5% ointment was, however, negative. A point that perhaps should be considered is that the use of greasy ointment bases on acutely inflamed areas of contact eczema transgresses against a general principle of dermatological therapy.

Other investigators have reported hydrocortisone to be of value in the acute phase of these reactions, but there was certainly no evidence of a general value of this nature in this series. Watery suspensions or lotions of hydrocortisone were not used.

This lack of response was disappointing because a local application of hydrocortisone ointment prior to applying a patch test with an agent already found to give a positive result produced a definite reduction in the reaction of 4 patients in this series so tested.

Pruritus Ani.

The results of treatment in pruritus ani were more encouraging. Of the 9 patients, 5 obtained considerable subjective relief. It is of interest that there was little objective evidence to support this declaration of subjective benefit, but 2 of the 5 patients certainly only obtained any relief at all while using the active ointment. Two others did not relapse when all treatment was omitted. As Malkinson and Wells have remarked, the response of patients to this measure often appears capricious, and in this group 4 apparently quite similar patients obtained no relief at all. Again, no general supportive measures were employed during the period of the investigation.

Cheilitis Exfoliativa.

Of the 5 cases of cheilitis exfoliativa, 3 obtained a very obviously significant benefit (to the extent of clinical cure) with hydrocortisone, but 2 relapsed when treatment ceased. Two other similar patients appeared to derive no relief.

Angular stomatitis.

Of the 3 cases of angular stomatitis, 2 were improved though not cleared.

SUMMARY.

A controlled clinical trial with hydrocortisone ointment is reported. 53 patients were treated.

The conditions in which it was used were : Flexural prurigo, infantile eczema, exogenous eczema, pruritus ani, cheilitis exfoliativa and angular stomatitis.

Hydrocortisone was of definite value in the treatment of cheilitis exfoliativa, and to a less degree, of angular stomatitis.

About one-half of the patients with uncomplicated pruritus ani experienced relief.

Hydrocortisone was not found to be of value in the treatment of exogenous eczema.

In a third of the cases of flexural prurigo and infantile eczema hydrocortisone had a limited beneficial effect, but the results did not suggest that by itself it was of great value.

My thanks are due to the Consultant Staff of the Manchester and Salford Hospital for Skin Diseases for permission to include patients under their care in this clinical trial, and for their encouragement in the investigation.

The 2.5% and 1% hydrocortisone ointments and the control ointment containing the base alone were kindly supplied in identical tubes for this investigation by Messrs. Upjohn of England Ltd.

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FIG. 1.—Case 1, aged 2 days.



FIG. 2.—Case 1, aged 10 days.



FIG. 3.—Case 1, aged 5 weeks.



FIG. 4.—Case 1, aged 12 weeks.



FIG. 5.—Case 1, aged 21 weeks.



FIG. 6.—Case 2, aged 3 weeks.

LAMELLAR DESQUAMATION OF THE NEW-BORN. ("COLLODION BABY").

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REPORTS of single cases do not as a rule serve much useful purpose in medical literature. Detailed reports of rare diseases, however, may be justified, especially if they have not hitherto been illustrated or described in detail. An infant born in Charing Cross Hospital may provide a case in point. He proved an interesting comparison with two other similar cases seen by us but not studied in such detail.

CASE REPORTS.

A male child, weighing 6 lb. 4 oz. at birth was born of a twenty-year-old mother in the thirty-eighth week of an uneventful pregnancy. It was the mother's second pregnancy. An elder daughter appeared normal and healthy, but nothing is known of the father as both children were illegitimate.

The mother appeared healthy, possessed of a fair skin of entirely normal texture and showing no congenital abnormalities. Her Wassermann reaction was negative at the thirty-second week of pregnancy. She suckled the child throughout its short life.

At birth it was noticed that the child's entire cutaneous surface was of a bright rose-red colour with the exception of the face and the pale tips of the fingers. The surface was shiny and presented the appearance, so aptly described, "as if painted with collodion." Within a few hours the skin of the face became as red as that of the rest of the body. Within twenty-four hours superficial cracks appeared in the "collodion" about the eyelids, forehead, mouth and lower trunk, and at the limb flexures, apparently from the movements of these parts. Respiratory excursion of the chest was not impaired and there was no difficulty in sucking. The lower eyelids were everted and there was some deformity of the ears. The external genitalia appeared normal and there was normal passage of urine and meconium.

During the next few days the cracks in the "collodion" covering extended and the surface was shed slowly in flakes of various sizes; these were firmly adherent and could not easily be pulled off. The less mobile parts of the skin were the last to shed this covering and the scalp retained it for several days. The remaining skin was seen to be of a dull matt red surface on separation of the flakes, and it appeared thickened but was soft to the touch. The finger- and toenails also appeared thickened. The scalp hair looked normal, but no eyelashes or eyebrows were present. At this stage it was considered that this was a case of so-called lamellar desquamation of the new-born (Fig. 1) and it was hoped that the skin would become normal in a few weeks. But this was not to be.

By the end of the first week the redness had almost completely disappeared and the skin had assumed a somewhat off-white colour. The skin now looked and felt dry and

harsh, and showed superficial cracks with scales of various size giving the appearance of ichthyosis. The whole skin surface, including the flexures, was affected and the ectropion was more marked. The slight deformity of the ears—a notching of the helix—became more obvious. The development of the scalp hair was normal. The nails grew very rapidly and remained thickened. No excessive sweating was observed. Scaling was most marked on the face and scalp. On the buttocks it was less conspicuous and the surface remained thickened and inelastic. Ectropion persisted and there was marked blepharo-conjunctivitis (Figs. 2-4).

For the first eight weeks the infant was kept naked in a warmed cot until light clothing was worn. Up to the eleventh week the skin was cleaned with sterile liquid paraffin and thereafter this was alternated daily with soap and water. Breast feeding continued, with iron and vitamin supplements. At the age of fifteen weeks he was allowed home (Fig. 5). General progress was maintained and he weighed 12 lb. at twenty weeks. The condition of the infant thus remained substantially unchanged



FIG. 7.—A portion of the "collodion" pellicle shed at the second week, showing the horn containing several layers of cells which has been lifted off the underlying epidermis. ($\times 870$).

when at the age of twenty-two weeks he died suddenly at home of fulminating broncho-pneumonia.

Two other cases have been seen. The second infant was seen through the courtesy of Dr. David Morris (Fig. 6). She showed similar appearances to the first case at birth, but the "collodion" pellicle peeled off and left the skin surface normal by the age of about six weeks. At the age of six months, when the child was last seen, the only cutaneous abnormality was a small ichthyotic patch on the right shoulder.

The third case was seen with Dr. D. J. Conway. It was a male infant, and the mother had had pre-eclamptic toxæmia. At birth the infant looked exactly like the infant in Charing Cross Hospital. The "collodion" pellicle had peeled off after about three weeks, and the ectropion had disappeared, but the skin remained rough and ichthyotic on the trunk and flexures (Fig. 7). This state of affairs persisted for six months, after which the child was not seen again, although a verbal message stated that the ichthyosis was still present at the age of one year.

PATHOLOGICAL FINDINGS (FIRST CASE).

Autopsy by Prof. W. St. C. Symmers showed skin appearances similar to those seen during life. No visceral abnormality was noted except in the res-

piratory tract which showed a bilateral acute severe broncho-pneumonia with numerous pleural petechial haemorrhages. Death was regarded as due to these changes.

Histological examination of the skin was made by Dr. Henry Haber, including examination of a piece of the "collodion" pellicle (Fig. 8) detached at two weeks and a biopsy at fourteen weeks, as well as the post-mortem study. The essen-

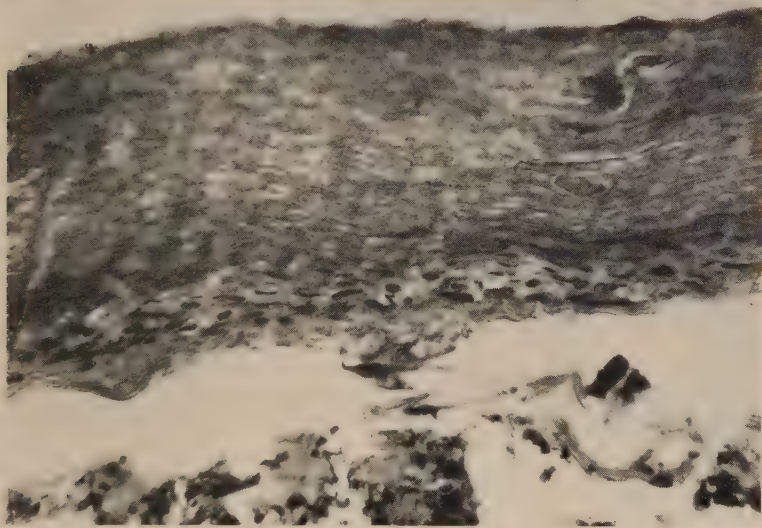


FIG. 8.

cial lesion is an epidermal abnormality. The findings may be summarised thus :

Stratum corneum.—A marked solid hyperkeratosis with desquamation of the horny layer in sheets. An uppermost cellular layer is differentiated as distinct from the stratum corneum and constitutes the "collodion" pellicle.

Stratum granulosum.—This is conspicuously thin, but with one or two layers of cells showing fine keratohyalin granules. There is a tendency towards vacuolation and pyknosis (Fig. 9).

Stratum spinulosum.—This is atrophic in places and shows acanthosis.

Corium.—Markedly cellular with inflammatory and fibroblastic elements. The lamellated elastic tissue shows an incompletely developed garland in some places.

The hair follicles and sweat ducts appear to have been distorted by the abnormality of the stratum corneum, resulting in an oblique, twisted ascent to the surface (Fig. 10).

The histological appearances are those of congenital ichthyosis with a superimposed epitrichial layer.

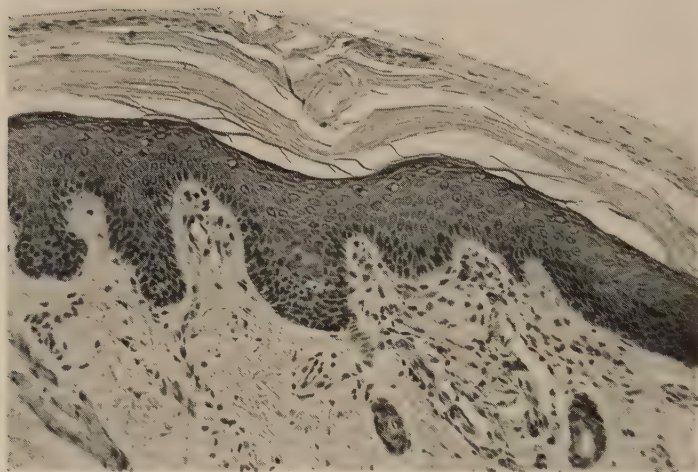


FIG. 9.—Skin of left thigh. $\times 320$. Stratum corneum throwing off uppermost layer of cells identical with "collodion" layer separated in early life. Stratum granulosum shows vacuolated cells. Rest of epidermis partly acanthotic and atrophic. A sweat duct is shown spiralling through stratum corneum.

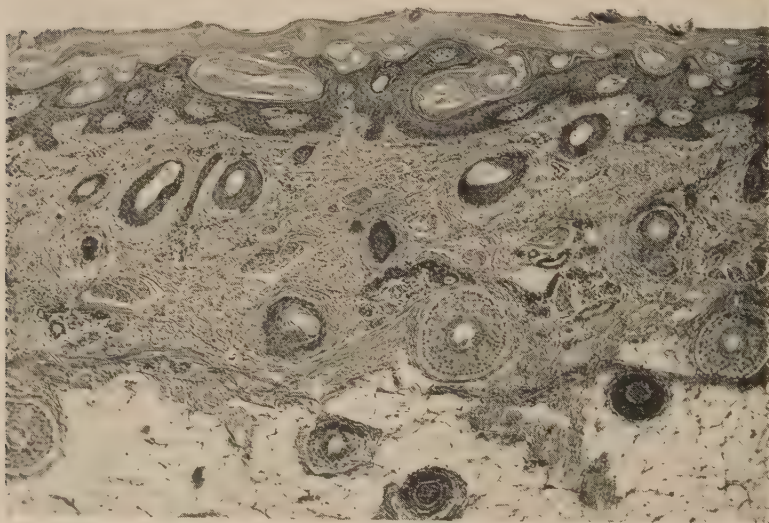


FIG. 10.—Skin of anterior scalp. $\times 150$. Thick solid stratum corneum containing hair follicles also showing hyperkeratosis and oblique arrangement. Stratum granulosum shows one or two layers of kerato-hyaline cells. The stratum spinosum is atrophic and acanthotic; rete pegs enclose islands of corium which is highly cellular.

DISCUSSION.

This type of case is usually classified as a form of ichthyosis. Indeed, Kaposi (1895) referred to it as ichthyosis sebacea. The first description seems to have been given by Perez (1880). Fox (1884) described the case of an infant boy deep red at birth, smooth and polished as if coated with varnish. The eyelids were fixed and everted. Cracks appeared at the flexures and after two weeks the skin, now scaly, peeled and left soft, pliable skin beneath. Plaques later developed on the head, trunk and flexures, and the child was subsequently exhibited as an "Alligator Boy" in an itinerant side-show. Fox called him a case of ichthyosis congenita. Nicolas and Moutot (1912) described a boy whose whole body was red at birth with his face seemingly painted with collodion. His brother was similarly afflicted and by the ages of ten and fourteen years both had developed severe ichthyosiform erythrodermia such as Brocq described in 1902. Grass and Torok (1895) mentioned a patient whose skin at birth was "smooth as satin". Finlay and Bound (1952) described an infant with similar collodion-like patches on the head and feet which recovered completely. Bonnet and Gaillard (1919), Bowen (1895), Dean (1921) and Carini (1895) described cases which took from several weeks to two years to recover. Dean's case was a girl whose mother and maternal aunt were said to have been affected. Tanissa (1949) and Tanissa and Nunes (1950) described and illustrated a brother and sister with the condition. These three families mentioned above are the only records found in the literature of familial incidence.

In some patients all, and in others only part of the skin surface was covered with "collodion". Some of the cases described by Kingsbury and Orel (Orel, 1929) showed typical collodion appearances at birth: later the skin became thickened and hard, and some of the infants died. A case described by Nicolas and Jambon (1909) showed collodion skin at first which gradually gave way to ichthyosis, and the "Alligator Boy" referred to by Fox was another case of ichthyosis.

Thus it seems that the collodion pellicle may involve any or all of the skin area. It may disappear completely in time or gradually give way to ichthyotic plaques—most commonly on the head and on the flexures. The redness also persists in these patients. In other words, the condition may progress to resemble Brocq's congenital ichthyosiform erythrodermia (CIE). This disorder is characterized by the appearance at birth or very shortly afterwards of erythrodermia and thickening of the horny layer to a greater or less degree and in many cases by rapid growth of the nails and hair. The hyperkeratosis persists into adult life and favours especially the face and flexures. Our first case showed rapid growth of the nails, and so did that of Nicolas and Moutot (1912). From the reports in the literature it is fair to say that some "collodion

babies" develop typical CIE and McKee and Rosen (1917) include some such cases in their review of that subject. Furthermore, they showed clearly that CIE is a different disease from the other forms of ichthyosis, although it should be classified in that wide group and although some cases may be difficult to place accurately. From a clinical point of view, therefore, "collodion baby" may be regarded as an early manifestation of CIE. Sometimes, indeed, it may be the only manifestation, together with the erythrodermia, of that condition. Lenglet (1902) considered the two conditions, CIE and ichthyosis, to be separate. He said that they were "of different evolution although of common origin and nature". It is certainly possible that one gene is responsible for all the signs—indeed, that is the implication we make—and equally possible that modifying factors may lead to modification of the ultimate clinical picture. Langlet's opinion may not, therefore, be at variance with our own. The answer to the question is unlikely to be found until much greater genetical knowledge is available.

There seems no reason to dispute the contention of Bowen (1895) that the shiny collodion pellicle is a persistence of the foetal epitrichium which normally develops at the second month of pregnancy and disappears by the sixth month. Beneath this pellicle the histology is typical of ichthyosis. McKee and Rosen maintain that the histology of CIE and other forms of ichthyosis are indistinguishable. The case studied by us in detail tends to support this.

SUMMARY.

A case of "collodion baby" is described and illustrated in detail, and reference is made to two other cases. From this small experience and a perusal of the literature, it seems that the disorder may be an early feature of congenital ichthyosiform erythrodermia (Brocq).

We wish to acknowledge the help of Dr. A. Doyne Bell, under whose care the first infant was treated in Charing Cross Hospital; to thank Dr. J. E. M. Wigley for his encouragement and help in preparing this paper and for his permission to publish the colour photographs and photomicrographs taken at The Institute of Dermatology by Mr. R. J. Lunnon; to thank Miss P. M. Turnbull for the colour photographs of the first case, Prof. W. St. C. Symmers for his autopsy report and Dr. Henry Haber for his histological examination. We also wish to thank Dr. David Morris for details of the second patient and the colour photograph, and Prof. D. J. Conway for particulars of the third case.

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MICROSPORUM CANIS INFECTION OF THE SCALP IN AN ADULT WITH CICATRICIAL ALOPECIA.

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THERE have been a number of reports of small-spore ringworm infection involving the scalp in adults. Pipkin (1952) has recently reviewed the literature and recorded his experiences of scalp ringworm in adults and adolescents. Of the small-spore infections *Microsporum canis* is more commonly encountered in this connection than *Microsporum audouini* and of Pipkin's 57 cases, which include nine small-spore infections, eight were *M. canis* and only one *M. audouini*.

Scarred alopecia has been described following infection with favus and some of the trichophyton ringworms. We are unable to discover any mention of scarred alopecia with microsporum ringworm.

CASE REPORT.

A housewife aged 42 attended hospital in September 1954. For two years she had had increasing loss of scalp hair, mainly on the vertex and frontal areas. Six weeks before she attended her son had developed ringworm, apparently from a cat in the household, and for a few days she had complained of scaly itching patches on her scalp. There had not been any other illnesses of note previously, or in her family. Her menses were regular.

Examination at this time showed over the vertex and frontal regions a large area of patchy alopecia with scarring; the appearances were typical of pseudo-pelade. On the left side there were, in addition, patches of scaling erythema which gave an obvious fluorescence under Wood's light. Microscopy showed typical small spores and culture revealed *M. canis*.

At first treatment was with Ung. Acid. Benzoic. Co. N.F. and when she was seen again after three weeks she had an extensive infection over the vertex and on the sides of the scalp away from the main areas of baldness. A 5% salicylamide ointment was then applied after washing with 1% Cetavlon. Three weeks later many of the areas were rather red and sore, but there was no fluorescence under Wood's light. Since this time the infection has remained clear, although the scalp is dry and scaly. The areas of scarred alopecia remain as before.

The association of *Microsporum canis* infection in an adult with scarred alopecia has three possible explanations. First, it may be pure chance, but

neither condition is very common and we think that this is unlikely. Second, the ringworm infection may have been present for many years and have gradually caused the scarring. This again is considered unlikely as scarring alopecia does not appear to have been described with *M. canis* infection; when first seen there was only one patch of the alopecia areas infected; after six weeks' treatment the infection cleared; and there is the coincidence of her son and her cat having patches at this time. Finally, the most likely explanation seems to be that the scarred alopecia altered the receptivity of the adult scalp to ringworm infection. This might be due to a reduction in the secretion of sebum and perhaps also to the fact that the sparse hair on the area might have allowed greater contact of the scalp skin with infecting material.

SUMMARY.

A woman with a two-year history of typical pseudo-pelade developed a *Microsporum canis* infection which cleared after six weeks' treatment. The association of a scarring alopecia and *M. canis* infection of an adult is discussed.

The patient was seen at Dr. Whitlock's clinic while he was away, and the authors have pleasure in expressing their thanks to him for the case notes and follow-up report.

REFERENCE.

PIPKIN, J. L. (1952) *Arch. Derm. Syph., Chicago*, **66**, 9.

CURRENT LITERATURE.

THE EFFECT OF TOPICAL APPLICATION OF VITAMIN A, WITH SPECIAL REFERENCE TO THE SENILE SKIN. F. REISS and R. M. CAMPBELL. (1954) *Dermatologica*, 108, 121.

Although vitamin A in massive doses by mouth has been used for years, with fair success in dermatoses showing dryness and hyperkeratosis, its topical use has received relatively little attention. Reiss and Campbell have used a cream containing 3000 i.u. to the ounce, and have noted distinct improvement in ichthyosis, lichen pilaris and pityriasis tabescentium. Psoriasis was not improved.

J. F. S.

STUDIES ON DRACONTIASIS AMONG YEMENITE IMMIGRANTS TO ISRAEL. I. KATZEN-ELLENBOGEN. (1954) *Dermatologica*, 108, 129.

Among 45,000 Jews who had emigrated from the Suda area of Yemen to Israel, there were found 68 cases of dracontiasis caused by *Dracunculus medinensis*. This infestation was previously unknown in Israel. The author gives a very full clinical and histo-pathological account of the disease, and also alludes to certain epidemiological problems.

J. F. S.

THEORETICAL AND PRACTICAL RESULTS FROM STUDIES OF EFFECT OF THIOLYCOLLIC ACID AND ALPHAMONOTHIOGLYCERIN ON HUMAN HAIR. H. RICHTER and W. FUHRMANN. (1954) *Arch. Derm. Syph., Berl.*, 198, 274.

Thioglycerin made alkaline with monoethanolamine should prove a valuable cold wave solution.

M. F.

RELATED DISORDERS OF SKIN, MUCOUS MEMBRANES AND OCULAR EPITHELIA. E. SCHRECK. (1954) *Arch. Derm. Syph., Berl.*, 198, 221.

First a differentiation is drawn between cutaneo-muco-oculo-epithelial and cutaneo-muco-ueval syndromes. The latter is not considered further. In the former conjunctiva and cornea may be involved. It is usefully further subdivided: for the various manifestations of erythema exsudativum multiforme, syndroma cutaneo-muco-oculo-epitheliale erythematum is suggested when the clinical picture comprises evanescent bullae; syndroma cutaneo-muco-oculo-epitheliale bullosum would include, as far as the eye is concerned, pemphigus ocularis vulgaris and pemphigus ocularis mucosus. Similar clinical pictures arise from drug allergy—syndroma cutaneo-muco-oculo-epitheliale allergicum. Epidermolysis bullosa hereditaria dystrophica may also affect the eye. Reiter's disease has a special place.

M. F.

BEHAVIOUR OF PROTEIN BOUND POLYSACCHARIDES IN THE SERUM IN DERMATOSES.**PART I: METHODS.** O. BRAUN-FALCO, W. WEBER and G. THAESLER. (1954) *Arch. Derm. Syph., Berl.*, 198, 585.

Disturbances in ground substance and cement substance in dermatoses might give changed values of serum polysaccharides or products of depolymerization. The technique employed in estimation of polysaccharides is described.

M. F.

BEHAVIOUR OF PROTEIN BOUND POLYSACCHARIDES IN THE SERUM IN DERMATOSES.**PART II: CLINICAL AND EXPERIMENTAL RESULTS.** G. WEBER, O. BRAUN-FALCO and G. THAESLER. (1954) *Arch. Derm. Syph., Berl.*, 198, 637.

In psoriasis, the increase in protein-bound carbohydrate resides in the albumin fraction mainly, and in addition slight increases of those linked to α_2 and γ globulin fractions were recorded. In eczema measurable rise occurs in the globulin fraction, in urticaria there is rise of hexoses; glucosamine values are normal. Other dermatoses tested in this way included lupus erythematosus, bullous eruptions, eczema solare and lichen planus.

M. F.

ON KELOID-LIKE SCLERODERMA, INCLUDING REMARKS ON VARYING BEHAVIOUR OF SCLERODERMATOUS CONDITIONS. G. W. KORTING. (1954) *Arch. Derm. Syph., Berl.*, 198, 307.

Microscopical and electronmicroscopical differences from keloid are described.

M. F.

MORPHOLOGICAL DELINEATION OF LICHEN PLANUS. H. OBERSTE-LEHN. (1954) *Arch. Derm. Syph., Berl.*, 198, 449.

Separation of epidermis and dermis is obtained by maceration. The morphology of the reliefs formed in this plane provides new material for a study of lichen planus. M. F.

DERMATOMYOSITIS AND REMARKS ON POIKILODERMA. H. A. GOTTRON. (1954) *Derm. Wschr.*, 130, 923.

The author stresses that poikiloderma is not a disease entity but an atrophic end-stage of various dermatoses. He discusses the pathology of dermatomyositis, and on the strength of the histological changes and various staining reactions suggests that circulatory derangements with altered capillary fragility lead to blood plasmaphoresis, the changes in the tissue ground-substance in cutis and musculature being secondary to this insudate.

The metachromasia (which disappears with hyaluronidase) he considered to be due not to hyaluronic acid but to chondroitin sulphuric acid. One reason adduced to support blood plasmaphoresis is the presence of subintimal swelling with metachromasia in the smaller arterial vessels without necessarily any metachromasia of the surrounding tissue. Another argument is the evidence of erythrodiapedesis in muscle tissue. M. S. S.

A MEDICAL TREATMENT FOR STASIS ULCERS. H. M. ROBINSON. (1955) *J. Amer. med. Ass.*, 157, 27.

The author believes that the importance of stasis as a factor in chronic leg ulcers has been over emphasized. He believes that bacterial invasion delays healing, although the organisms isolated from leg ulcers are usually saprophytic or only doubtfully pathogenic. Seventy-two patients with leg ulcers were treated with antibiotics in powder form and in 71 the ulcers were healed within 8 months. Patients were advised to rest, but many were unable to do so. It is not stated what form of bandaging was employed. Dermatitis developed in some cases. (The author does not refer to the work or concepts of Bauer, Bisgaard or Anning. He mentions that varicose veins were present in only 20% of his cases, but does not point out that gross venous stasis may be present in the absence of superficial varicosities.) A. J. R.

TREATMENT OF JUVENILE MELANOMAS AND MALIGNANT MELANOMAS IN CHILDREN.

H. E. McWHORTER, F. A. FIGI and L. B. WOOLNER. (1954) *J. Amer. med. Ass.*, 156, 695.

The authors review the "melanomas" in children in the Mayo Clinic files. They were able to confirm that the juvenile melanoma and the malignant melanoma in childhood are distinct lesions with a very different prognosis. The juvenile melanoma must also be differentiated from the common pigmented naevus although it is possible that if left undisturbed many juvenile melanomas mature into quiescent intradermal naevi in later life.

There were 11 juvenile melanomas occurring in children between the ages of 1 and 9. The authors have occasionally seen these lesions in adults. The tumours were commonest on the head, especially the cheeks, and ranged in size from 4 mm. to 1 cm. in diameter. Most had been present for less than a year. They were usually elevated, pink or red in colour and unpigmented. The critical histological feature is the presence of large cells of the type seen in melanomas but lacking anaplastic changes. All 11 patients were followed up and were found to be free from recurrences. Treatment had in some cases been limited to simple excision.

Only 5 children under 12 with malignant melanoma were seen at the Mayo Clinic from 1907 to 1949. Four of the 5 lesions were on the face or ear. Four of the patients died of the disease, but the fourth is well 21 years after surgical treatment. The histological features of these cases were unquestionably malignant with gross anaplastic changes. The authors consider that malignant melanoma in childhood does not differ from the same disease in the adult. Most statements to the contrary are the result of confusion with juvenile melanoma. In the treatment of malignant melanoma wide surgical excision, followed if necessary by grafting, is recommended, but the regional lymph nodes should be dissected only if they are enlarged. Simple local excision is sufficient for the juvenile melanoma. A. J. R.

AVASCULAR NECROSIS OF THE PHALANGES OF THE HANDS (THIEMANN'S DISEASE).

E. W. SHAW. (1954) *J. Amer. med. Ass.*, 156, 711.

Thiemann's disease is an uncommon condition, not strictly within the province of the dermatologist but which might be encountered incidentally in dermatological practice. The disease is inherited and is usually first clinically apparent in late childhood. As the result of avascular

necrosis of the phalanges there is enlargement of the interphalangeal joints and shortening of the fingers. The author reports 4 probable and 18 possible cases in six generations of a family and gives a short account of the clinical and radiological features.

A. J. R.

CORTISONE TREATMENT OF SARCOIDOSIS. H. L. ISRAEL, M. SONES and D. HARRELL. (1954) *J. Amer. med. Ass.*, **156**, 461.

Thirty-six patients with sarcoidosis were treated with cortisone. The majority received 200 mg. daily for the first 10 days. In 11 patients the dosage was rapidly reduced and discontinued. In 19 patients, the dosage was gradually reduced over periods of 1-4 months, but in 5 patients with severe respiratory disability the cortisone has been continued for 1-2 years. Although the course of the disease was seldom favourably influenced and 4 patients died of progressive sarcoidosis, symptomatic improvement, often considerable, was noted in 35 cases and was frequently maintained after treatment was discontinued. Benefit was most striking in extra-pulmonary manifestations of short duration. Improvement in pulmonary lesions was less frequent and there was no significant effect on mediastinal lymphadenopathy.

A. J. R.

MANGO DERMATITIS. L. C. GOLDBERG. (1954) *J. Amer. med. Ass.*, **156**, 954.

Two cases of mango dermatitis are reported. A perioral dermatitis develops after eating the fruit in patients who are sensitive to the resin-like substance—cardol—present in the peel. There may possibly be cross sensitivity between cardol and urushiol, the toxic principle of poison ivy.

A. J. R.

ENVIRONMENTAL FACTORS OF OCCUPATIONAL ORIGIN RELATED TO CARCINOGENESIS. I. MACDONALD. (1955) *J. Amer. med. Ass.*, **157**, 5.

A general review of our present knowledge of carcinogenic occupational hazards. Most dermatologists would not agree that either verruca or scleroderma could be accepted as "lesions that may be associated with occupational carcinogens".

A. J. R.

A NEW TYPE OF PRESSURE DRESSING FOR HYPOSTATIC DERMATITIS. M. REITSCH and F. C. COMBES. (1955) *J. Amer. med. Ass.*, **157**, 36.

This new type of dressing is made from a sheet of foam rubber and is fitted with a zip-fastener. It is adjustable and extends from the malleoli to below the knee, but gives no support behind the malleoli.

A. J. R.

ACQUIRED AGAMMAGLOBULINEMIA. REPORT OF THREE CASES. H. H. ZINNEMAN, W. H. HALL and B. I. HELLER. (1954) *J. Amer. med. Ass.*, **156**, 1390.

Since the first case of agammaglobulinemia was described by Bruton in 1952 several others have been reported and the condition may not be very rare. In agammaglobulinemia the serum protein fractions are normal with the exception of gammaglobulin which may be absent or present in amounts that can be detected only by immunological methods. Clinically the condition is manifest by extreme susceptibility and no antibody response to infections. In most of the reported cases children with a history of recurrent bacterial infections, such as pyoderma, otitis media, sinusitis or purulent arthritis, have shown a normal response to antibiotics but have relapsed as soon as treatment was stopped. In one case a virus infection was involved and fatal generalized vaccinia developed after the vaccination of a girl aged 11 months.

There are apparently two groups of cases: those which are idiopathic and possibly congenital and those secondary to extensive disease of the lymphatic or reticulo-endothelial systems. Three new cases in adults are reported. In one patient the condition was probably secondary to generalized sarcoidosis, but the cause in the other two could not be discovered although it was apparently acquired in adult life. In the patient with sarcoidosis biopsies of liver, spleen and lymph nodes showed an absence of plasma cells, which may be significant if these are, as some believe, the source of gammaglobulin.

A. J. R.

ERYTHEMA MULTIFORME EXUDATIVUM (STEVENS-JOHNSON SYNDROME). D. A. MAURIELLO. (1954) *J. Amer. med. Ass.*, **156**, 1495.

The author presents a clinical report on 14 cases of Stevens-Johnson syndrome seen in an Army hospital in eighteen months. There were no unusual features. Eight patients were treated with

either ACTH or cortisone, which seemed of doubtful value. Antibiotics appeared to have no effect other than the control or prevention of secondary infection. A. J. R.

THE CLINICAL COURSE OF SYSTEMIC LUPUS ERYTHEMATOSUS. P. A. TUMULTY. (1954) *J. Amer. med. Ass.*, **156**, 947.

This long and valuable article based on 105 patients studied at Johns Hopkins Hospital should be read in the original and only a few points can be selected for mention in a short abstract. Although the majority of patients were women aged between 11 and 50 there were 4 patients under 10 and 4 over 61, and 23 were males. The course of the disease was frequently less rapid and was less uniformly fatal than some shorter series of cases suggest. The average duration of illness was 7 years, and although some patients survived only a few months, some were alive after the disease had been present from 15 to 20 years and perhaps longer. The excellent review of the clinical manifestations emphasizes their almost infinite variability and hence the great importance of laboratory findings, which are critically discussed. An abnormal electrophoretic pattern of the serum proteins may be of diagnostic assistance. A. J. R.

ATHEROSCLEROSIS AND AORTIC STENOSIS IN HYPERCHOLESTEREMIC XANTHOMATOSIS. D. P. BAER, S. ROTHBARD and H. A. EDER. (1954) *J. Amer. med. Ass.*, **156**, 943.

A boy of Greek parentage developed xanthomatosis at the age of 4. Three years later an apical systolic murmur was detected and his serum cholesterol was found to be 400 mg./100 c.c. The xanthomata gradually became more numerous and prominent. From the age of 13 angina and dyspnoea became increasingly severe and he died at the age of 20. He was found at autopsy to have unusually extensive atherosclerosis involving not only the aorta and its main branches but three of the heart valves and the endocardium. There was an extreme degree of aortic stenosis with calcification. The literature on the cardiovascular lesions associated with xanthomatosis in early life is briefly reviewed. A. J. R.

GRANULAR CELL MYOBLASTOMA OF THE VULVA. W. J. REICH, A. M. DOSWALD, P. C. WILLIAMS and M. J. NECHTOW. (1954) *J. Amer. med. Ass.*, **156**, 714.

Granular cell myoblastoma of the vulva is very rare. In the reported case a non-tender nodule on the right labium majus of a negro woman aged 33 had been present for four years and was 1.3 cm. in diameter. These lesions are radio-resistant and should be excised. A. J. R.

REPORT PREPARED BY THE COMMITTEE ON OCCUPATIONAL DERMATOSES OF THE COUNCIL OF INDUSTRIAL HEALTH OF THE AMERICAN MEDICAL ASSOCIATION. (1954) *J. Amer. med. Ass.*, **156**, 497.

This is an informative and straightforward account of patch-testing techniques and the critical evaluation of results. A. J. R.

EPIDERMAL PROTEASE. G. C. WELLS and C. BABCOCK. (1953) *J. invest. Derm.*, **21**, 459.

Epithelial cells have some proteolytic action on fibrin in the healing of wounds. Autoproteolysis is supposed to be one of the factors in the formation of bullae in skin damaged by vesicants. According to the results of the present work most of the skin proteinase described by Beloff and Peters must have been derived from the epidermis. Plasma contains an inhibitor. J. H. T. D.

LIVER VITAMIN A IN DARIER'S AND DEVERGIE'S DISEASES. T. CORNBLEET. (1954) *J. invest. Derm.*, **23**, 71.

For a short succinct and exhaustive account of the dermatological aspects of vitamin A and its metabolism expressed in clear though not particularly elegant English this article is recommended; both to the reader who wishes to know about vitamin A and to the writer needing reassurance that style is not indispensable for the communication of ideas. J. H. T. D.

THE EFFECT OF CANDICIDIN ON INTERTRIGINOUS AND PARONYCHIAL MONILIASIS. A. G. FRANKS, C. L. TASCHDJIAN and G. A. THORPE (1954) *J. invest. Derm.*, **23**, 75.

In the absence of any explanation it would appear to have been taken for granted that the chronic inflammation of the nail folds commonly seen in dermatological clinics is primarily a monilial infection.

Simultaneous paired comparisons are supposed to have been made "where feasible", but they are not mentioned in the results. Otherwise not the slightest hint of a control.

J. H. T. D.

A MICRO-METHOD FOR THE ESTIMATION OF FREE AND COMBINED CHOLESTEROL USING THE MONOLAYER FILM TECHNIC. A. C. KEYL and K. K. JONES. (1954) *J. invest. Derm.*, 23, 17.

Of interest to the biochemist.

J. H. T. D.

VIABILITY OF COCCIDIODES IMMITIS. I. ISOLATION FROM A SEVEN-MONTH-OLD SEALED MICROSCOPE SLIDE. R. C. BURKE. *J. invest. Derm.* 23, 1.

The slide had a smear of pus obtained at autopsy cover-glassed and ringed with Tufon No. 74. Having survived for six months an adventurous existence in the luggage of a travelling lecturer the microbe was noticed to be attempting to escape.

J. H. T. D.

A STUDY OF THE BLOCKING EFFECT OF PLASMA AND OF LYSED RED BLOOD CELLS ON DELAYED ALLERGIC REACTIONS. A. ROSTENBERG and G. J. BREBIS. (1954) *J. invest. Derm.*, 23, 3.

It has been suggested that the positive anergy to tuberculin of patients with sarcoidosis must be due to something in the plasma which prevents the reaction by combining with the antigen. These experiments confirm the probability of its existence, but show that there is perhaps more of it in the red cells than in the plasma. It appears to be rather a variable quantity in that a given sample is not specific for any particular antigen and its performance varies greatly in respect of different recipients. There does, however, appear to be more of it in the blood of sarcoidosis cases than of others.

J. H. T. D.

HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. VI. THE DISTRIBUTION OF SULPHYDRYL AND DISULPHIDE GROUPS. W. MONTAGNA, A. Z. EISEN, A. H. RADEMACHER and H. B. CHASE. (1954) *J. invest. Derm.*, 23, 23.

The stain of Barnett and Seligman is employed with paraffin sections.

J. H. T. D.

STUDIES ON THE THERAPEUTIC EFFECT OF TRYPSIN. B. HEILESEN. (1954) *J. invest. Derm.*, 23, 7.

It is evidently useful for the removal of sloughs. The process is sometimes painful and should be employed with great caution in arteriosclerotic ulcer.

By "varicose ulcer" it is supposed that the author means the common postphlebotic ulcer and not some comparatively rare complication of varicose veins. Greatly to be admired in this paper is the succinct and clear method of case presentation.

J. H. T. D.

THE PROPERTIES OF THE RECEPTORS IN THE AXON REFLEX SWEATING PRODUCED BY NICOTINE AND SODIUM CHLORIDE. M. WADA. (1954) *J. invest. Derm.*, 23, 63.

The pharmacological study of axon reflex sweating concerns the capacity of certain drugs to inhibit the action of hypertonic NaCl and nicotine at the receptor end, to block the afferent nerve impulse or, by interfering, for example, with the liberation of acetyl choline, to stop the reaction at the effector end.

These experiments are mainly concerned with the first of these; and a great variety of substances were mixed with the axon reflex-provoking agent. Of these "TEA" hexamethonium and decamethonium blocked the response to nicotine but not to NaCl; and ten times as much procaine banthine ephedrin and tubocurarine were needed to block the response to NaCl as to nicotine. On the whole the receptors of the axon reflex resemble those of autonomic ganglion cells rather than those of motor end-plates; with the important reservation that potassium ions and pilocarpine, though stimulant of the latter, inhibit the axon reflex.

J. H. T. D.

TRICHOSTASIS SPINULOSA. E. LADANY. (1954) *J. invest. Derm.*, 23, 33.

Of 200 ordinary comedones, including "free flowing transparent sebaceous plugs which contained no or few cellular elements" only 15% had no lanugo hairs in them at all. In 16% there were more than 3 hairs. It is therefore proposed that "trichostasis spinulosa" be regarded as no more than a special form of comedo.

J. H. T. D.

THE RELATIONSHIP BETWEEN THE DOWNY AND GRANULAR FORMS OF TRICHOPHYTON MENTAGROPHYTES. L. K. GEORG. (1954) *J. invest. Derm.*, **23**, 123.

T. mentagrophytes derived from acute lesions on exposed parts generally makes a granular colony, from the interdigital webs a downy one. The former has greater pathogenicity and virulence, but the latter can be stepped up in both respects by passage, and this is sometimes associated with a return to the granular form.

The woolliness of the colony is not the same thing as pleomorphism, in which state there is developed a characteristic mycelium of small calibre and incapable of forming spores. While pleomorphism occurs readily in the granular colonies it is only obtained with difficulty in the downy ones; but when it does occur it is distinguishable by the naked eye. J. H. T. D.

THE SURFACE TENSION OF HUMAN SWEAT; ITS DERIVATION AND ITS SIGNIFICANCE.

W. C. RANDALL and C. CALMAN. (1954) *J. invest. Derm.*, **23**, 113.

The surface tension of chemically pure water is 71.8 dynes per sq. cm., of Ringers solution 74, of sweat as it issues from the pore 69.25, and as scraped off the skin 65. This last difference is about as much as that obtained in water by adding 1 per 1000 of a well-known detergent. Although lowering of surface tension has little effect on the rate of evaporation it clearly promotes it by facilitating the flow over the surface. J. H. T. D.

CLINICAL EVALUATION OF DIPARALENE IN THE MANAGEMENT OF TINEA CAPITIS.

M. W. ROSENTHAL, C. W. DAESCHNER and W. J. FAHLBERG. (1954) *J. invest. Derm.*, **23**, 119.

Diparalene is an antihistaminic that has been found to be fungistatic *in vitro*.

The number of cases is too small to justify any conclusion as to its value, though it did seem that the 5% ointment was a trifle more effective than the 2%. J. H. T. D.

FREQUENCY CURVE STANDARDS IN THE EVALUATION OF DERMATOLOGIC THERAPY.

J. T. CRISSEY. (1954) *J. invest. Derm.*, **23**, 85.

The mathematical formulae cluttering the pages of this excellent paper are unnecessary either to the demonstration or to the argument, but they will no doubt guarantee to some minds the correctness of the observations on pityriasis rosea and alopecia areata.

The author urges that the temptation to employ for self-limiting or incurable diseases remedies no more effective than the average but capable of producing such unwelcome side effects as peripheral neuritis, hepatitis, agranulocytosis and death, might be reduced if we all knew more about the natural courses of the diseases we have to pretend to treat.

Unfortunately a naive faith in the remedies which happen to be in fashionable demand has become indispensable for even the most modest material success in medicine, and it would be unfair to both sorts of physician to make this kind of knowledge too readily available: so let us leave it encrusted in its hieroglyphics. J. H. T. D.

THE INFLUENCE OF SOME VITAMIN DEFICIENT DIETS ON A SUBSTANCE CHARACTERISTIC OF THE EPIDERMIS OF THE MOUSE, RAT AND MAN. C. CARRUTHERS and V. SUNTZEFF.

(1954) *J. invest. Derm.*, **23**, 77.

Some rats having been sacrificed with elaborate dietetic and other ritual, the oracle makes the pronouncement that the substance which is supposed specifically to disappear from the tissue with the development of a squamous carcinoma "... is polarographically reducible, and its reduction at the dropping mercury electrode resembles that of some pyridine compounds, but the substance from epidermis does not have the same half-wave potential as pyridine compounds known to occur in animal tissues. Furthermore, its absorption spectrum is different from that of the pyridine compounds examined (in some cancer research by the same authors). The absence of a tertiary or quaternary nitrogen in the reducible substance ..." and "Although it is present in minute amounts in epidermis attempts are underway to isolate this substance in crystalline form to facilitate further characterization by physico-chemical means."

We wouldn't have minded waiting a bit ourselves. J. H. T. D.

THE CHEMISTRY OF CERUMEN. L. AKOBYANOFF, C. CARRUTHERS and B. H. SENTURIA. (1954)

J. invest. Derm., **23**, 43.

This is the detailed record of an attempt to identify some of the fatty acids of cerumen. Only about 5% of fresh cerumen is saponifiable ether soluble lipoid, but the impressive quantity of 28.5 gm. of ear-wax had been collected and preserved in the deep freeze for this experiment.

Though preliminary work had confirmed that chromatography, using 94% methyl alcohol as the solvent, gave good separation for fatty acids within the expected range and an indication of values down to 0.01 mg., the results here were disappointing.

J. H. T. D.

HISTOLOGY AND CYTOCHEMISTRY OF HUMAN SKIN. IV. THE ECCRINE SWEAT GLANDS.

W. MONTAGNA, H. B. CHASE and W. C. LOBITZ. (1953) *J. invest. Derm.*, 20, 415.

An aesthetically satisfying account of the histochemistry of axillary eccrine glands only very slightly marred by spelling mistakes and the use of such neologisms as "ductual".

J. H. T. D.

A DWARF FORM OF MICROSPORON GYPSEUM. C. A. FUENTES, R. ABOULAFIA and R. J. VIDAL. (1954) *J. invest. Derm.*, 23, 51.

This organism was isolated from a kerion in a small boy. The hair shaft showed invasion of the favus type. The colony characteristics were those of a fast growing *M. gypseum*, but the macroconidium differed conspicuously from the usual in being of less than a quarter its size, having only one septum and a surface covered with spines. The fungus grew on hair and nails *in vitro* and produced lesions in animals and man but, under experimental conditions, without invasion of hair.

J. H. T. D.

A SPECTROPHOTOMETRIC TEST IN ATTEMPTS TO DIFFERENTIATE PEMPHIGUS SERUM FROM THAT OF OTHER BULLOUS DISEASES. H. A. COHEN and C. R. REIN. (1954) *J. invest. Derm.*, 23, 143.

The addition of 0.5 c.c. of normal serum to 5 c.c. of sodium acetate buffer solution containing bromthymol blue reduces the absorption of light between 500 and 700 m μ ; but some thermolabile characteristic of pemphigus serum reduces it still further, flattening out completely the last relics of the peak at 615 m μ peculiar to the dye.

Whether the immediate cause is some "X factor", some alteration in the colloidal structure, haemolysis, or qualitative changes in the plasma protein, it does not seem to be directly related to the albumin-globulin ratio.

Though the reaction was absent in a small number of patients seriously ill with grave systemic diseases, it did occur in 4 out of 25 cases of D.H.; and, out of a control series of 186 cases representing 105 non-bullous dermatoses, in 3 cases of L.E. taking mepacrin, 3 of pityriasis rosea, one of psoriasis having treatment with tar and U.V.R. and a handful of Wassermann-twisters. Of 15 active cases of pemphigus vulgaris only one, and one very active chronic case of pemphigus foliaceus, yielded normal curves.

The control series has evidently been designed to include a maximum number of distinct diagnostic entities, but the names of 83 of them are not given. It appears to have included only one case of eczema but, presumably in lieu of normal subjects, as many as 15 of acne vulgaris and 28 of contact dermatitis.

J. H. T. D.

THE CHESTERFIELD MEDAL.

The form of the Chesterfield Medal examination has now been changed. From this year the Chesterfield Medal with a cash prize of £25 will be awarded to the applicant submitting the best essay on a dermatological subject selected by himself. The essay should preferably not exceed 5,000 words. Candidates must hold a medical qualification (of any country) and must not be of accepted consultant status. The examiners may require any of the candidates to attend for interview. The closing date for this year's examination will be 30th September. Further details may be had on application to the Dean, The Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, London, W.C.2.